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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/125,953	12/10/98	FODSTAD	7885.56USWO

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MERCHANT & GOULD P.C.
P.O. BOX 2903
MINNEAPOLIS MN 55402

EXAMINER	
SISSON,B	
ART UNIT	**PAPER NUMBER**
1655	24

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/125,953	FODSTAD ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 3, 5-9, and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-9 and 12* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claim 5 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 requires that the cells be isolated. Claim 12, the independent claim from which claim 5 depends, requires that one repeatedly immunomagnetically isolate the target cells. Seemingly, the cells are already as isolated, as one would have them upon completion of step "B."

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2, 3, 5-9 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Upon review of the disclosure it is noted that in none of the experiments provided (Examples 1-4 at pages 5-7 of the specification) that none of the reaction conditions are set forth. At page 6, first paragraph, it is noted that reference has been made to certain journal articles as to how differential display was conducted. At page 4, last paragraph, reference has been made to a PCT publication as disclosing methods for the positive selection of target tumor cells. Further

review of the specification fails to find any indication that the articles had been incorporated by reference. Assuming *arguendo*, that the articles had been incorporated by reference, the present specification would not satisfy the requirements of enablement as set forth under 35 USC 112, first paragraph, as the incorporation by reference of essential subject matter without such subject matter being in a cited US patent is prohibited. Accordingly, the subject specification is essentially silent as to what reaction conditions and starting materials are used in practicing the full scope of the claimed methods. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
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> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a</u>

> failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

4. Claim 2 further defines claim 12 as allowing the simultaneous screening of 12 or more different samples. The specification clearly does not present such a showing and as such, the specification does not enable the identification of one or more genes when the starting can be in a cell and/or be a mixture of nucleic acids from a variety of tissues.

5. Claims 2, 3, 7-9 and 12 have sufficient breadth of scope so to encompass conducting the assay either *in vivo* or *in situ*. The specification, however, is essentially silent as to how such methodologies are to be applied. The specification provides four examples with examples 2-3 being built upon that of Example 1. As set forth in Example 1, RNA was first extracted from the immunomagnetically-separated cells (one pass). Applicant is seemingly relying upon one of skill in the art to determine how such embodiments are to be practiced. Such reliance upon the public for enablement, and not that of the specification, is an unfair shifting in the duty of full and complete disclosure as to how one is to make and use the claimed invention.

6. Similarly, language in claim 7 that the method is to encompass "any other procedure that can be used to identify genes with differential expression" broadens the claim tremendously and clearly is not enabled by the specification.

7. Claim 8 requires one to perform sequencing reactions, identify "interesting site-specific or site-preferenced patterns". The specification is essentially silent as to how one is to proceed in recognizing such sites and evaluating them.

8. Claim 9, which depends from claim 8, is similarly not enabled by the disclosure as it relates to studying the pattern of expression for the "identified genes." It is noted that the subject disclosure does not set forth a repeatable procedure whereby any gene has actually been identified and is subsequently studied. Without something to guide the skilled artisan, the skilled artisan must resort to undue experimentation to practice the claimed invention.

9. For the above reasons, and in the absence of convincing evidence to the contrary, the subject specification has not been found to enable the claimed invention and as such, claims 2, 3, 5-9 and 12 have been rejected under 35 USC 112, first paragraph.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 2, 3, 5-9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 6 provides for the use of the extracted nucleic acids, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

13. Claim 6 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

14. Claim 8 is indefinite with respect to just what constitutes "interesting site-specific or site-preferenced patterns."

15. Claim 9 is indefinite with respect to just what constitutes "relevant tumor sites."

16. Claim 12 is confusing as a result of the presence of more than one period occurring in the claim, e.g., the periods that follow A, B, C, etc. Applicant is urged to consider using a parenthesis after such identifiers. Claims 2, 3, and 5-9, which all depend from claim 12, fail to overcome this issue.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 2, 3, 5-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Høifødt et al., in view of Smith et al. (US Patent 5,776,683).

Høifødt et al., disclose immunomagnetic separation of target sells that can be isolated from tumors. The cells are subsequently subjected to "further various experiments" (page 1). Page 3, and pages 6-8, teach how one can immunomagnetically separate cells. Page 5 teaches that the method of separating cells allows for the detection and isolation of cells associated with various cancers, including those that are metastatic. Page 8 teaches explicitly that the cells may be derived from "malignant cells present in mammalian tissues, for example bone marrow, peripheral blood, pleural and peritoneal effusions, and other bodily fluids, for example urine, cerebrospinal fluid, semen, and lymph. Studies involving polymerase chain reaction (PCR) methodology will also gain in specificity and reliability when preformed on pure tumor cell populations obtained by the new method."

Høifødt et al., does not teach conducting differential expression analysis nor the isolation and identification of genes present in the isolated cells.

Smith et al., amplification of cDNA derived from isolated cancer cells and differential expression analysis of same. See columns 8 and 17-19. As seen therein, the method can be adapted so to permit the analysis of two or more cancer cell types at one time. Column 20 teaches the isolation of selected expressed genes and the subsequent cloning and studying of same.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the method of Smith et al., with that of Høifødt et al., as such would have afforded the ordinary artisan with and enhanced capacity to isolate cancer cells and to then conduct differential gene expression analysis as Høifødt et al., teaches explicitly of the benefits of combining their method with that of PCR analysis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
April 26, 2001